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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/142,095	11/02/1998	BRIAN BURCHELL	MUR-7450	1739

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EXAMINER
TAYLOR, JANELL E

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/142,095	Applicant(s) BURCHELL, BRIAN
	Examiner Janell Taylor Cleveland	Art Unit 1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 2-14 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 2-12 and 14 is/are rejected.

7)☒ Claim(s) 13 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The following is a FINAL REJECTION, necessitated by amendment. Any rejection not reiterated is withdrawn. A Response to Arguments section follows.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bosma et al. (New England Journal of Medicine, Vol. 333 No. 18, pages 1171-1175) in view of Stratagene Catalog (1988, page 39).

The claim is drawn to a kit for screening participants for clinical drug trials, wherein the kit comprises primers for amplifying a region of DNA indicating a genetic basis of Gilbert's Syndrome, and the kit further comprises instructions directing a user of the kit that the kit should be used to identify drug trial participants having the genetic basis for Gilbert's Syndrome.

Bosma et al. teaches the genetic basis of the reduced expression of bilirubin UDP-glucuronosyltransferase 1 (UGT1) in Gilbert's Syndrome. Bosma et al teaches that this region may be amplified by primers, which are specific for the region associated with Gilbert's Syndrome. (Page 1172, first column, last two paragraphs.)

Bosma does not teach instructions for use along with the primers.

Stratagene teaches kits with primers, and the kits come with instructions.

It would have been obvious to combine the teachings of Bosma with those of Stratagene. This is because instructions would have been useful in instructing the practitioner how to use the primers to amplify the subject material.

In regards to what the instructions actually teach, they are given no "patentable weight" in terms of what the instructions are drawn to. In re Gulack (CAFC) 217 USPQ 401 relates to a measuring cup. In the case of In re Gulack, the printed matter is considered a patentable distinction because the function of the device depends upon the printed matter itself, which is a part of the substrate; without the printed indicia or numbers, the substrates lose their function. Such is not the case with the instantly claimed kit. The components of the kit remain fully functional absent the printed instructions for use. Thus the instructions for use included in a kit or article of manufacture constitute "intended use" for that kit or article of manufacture. Intended used does not impart patentable weight to a product. See MPEP 2111.03:

> Intended use recitations and other types of functional language cannot be entirely disregarded. However, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey 370 F.2d 576, 152 USPQ 235 (CCPA 1967); In re Otto, 312 F.2d 937, 938, 136 USPQ 458, 459, (CCPA 1963).

In the instant case, the claims are drawn to a kit comprising instructions, and primers. The intended use which is recited on the instructions lacks a functional relationship to the kit because the instructions do not physically or chemically affect the chemical nature of the components of the kit, and furthermore, the components of the kit can still be used by the skilled artisan for other purposes (as a whole or individually). Therefore,

the kit is unpatentable over the prior art because they function equally effectively with or without the instructions, and accordingly no functional relationship exists between the instructions for use and the kit components.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 2-11 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosma in view of Sibille et al (Eur. J. Clin. Pharmacol. Vol. 39, pages 475-479, 1990).

Claim 2 is drawn to a method for screening individuals for participation in clinical drug trials, the method comprising the steps of: a) collecting a sample from each an individual, b) screening the samples for the genetic basis of Gilbert's Syndrome, c) determining if the individual has the genetic basis of Gilbert's Syndrome, and d) proceeding with the clinical drug trial based on the knowledge of such individuals possessing or not possessing the genetic basis of Gilbert's Syndrome. Claim 3 is drawn to the sample containing DNA from the individual. Claim 4 is drawn to the test of claim 1 wherein the method further comprises the step of eliminating participants having the genetic basis of Gilbert's Syndrome from the clinical drug trial. Claim 5 is drawn to the test of claim 1 wherein the method further comprises the step of selecting only participants on having the genetic basis for Gilbert's Syndrome for the clinical drug trial.

Claim 6 is drawn to the test further comprising the step of interpreting the results of the clinical drug trial based on the knowledge that certain participants have the genetic basis of Gilbert's Syndrome as distinguished from participants adversely affected by the drug. Claim 7 is drawn to the method of claim 1 wherein the method comprises the steps of: a) isolating DNA from each sample; b) amplifying the DNA inner region indicating the genetic basis of Gilbert's Syndrome; c) isolating amplified DNA fragments, and d) identifying individuals having the genetic basis for Gilbert's Syndrome. Claim 8 is drawn to the use of radioactively labeled pairs of primers. Claim 9 is drawn to the genetic basis for Gilbert's Syndrome being the gene of UGT. Claim 10 is drawn to the DNA to be amplified coming from the UGT1 exon 1 region. Claim 11 is drawn to the DNA to be amplified coming from the region between –35 and –55 nucleotides at the 5' end of UGT 1 exon. Claim 14 is drawn to the method of claim 2 wherein the sample is a blood sample or a buccal smear sample.

Bosma et al. teaches the genetic basis of the reduced expression of bilirubin UDP-glucuronosyltransferase 1 (UGT1) in Gilbert's Syndrome. Bosma et al teaches that this region may be amplified by primers, which are specific for the region associated with Gilbert's Syndrome, particularly the promoter region which is found at the intron-exon junction of UTP1. (Page 1172, first column, last two paragraphs.)

Bosma et al does not teach a test in clinical drug trials which involves screening of the genetic basis for Gilbert's Syndrome.

Sibille et al. teaches a laboratory screening method for the selection of healthy volunteers. Specifically, Sibille teaches "the aim of laboratory screening in phase I is to

exclude subjects with subclinical illness, who might be at increased risk in the study, and who might also adversely influence interpretation of the results." (Summary). Furthermore, Sibille et al teaches screening on the basis of abnormal levels of bilirubin, which is found in patients with Gilbert's Syndrome. (Table 3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Bosma and Sibille. This is because, as Sibille taught, it would have been beneficial to remove those from a drug trial whose illness might adversely affect the outcome of the results. Furthermore, it was known that abnormal levels of bilirubin would have affected the outcome of clinical drug trials. It would have been obvious to screen participants for Gilbert's Syndrome, as this condition would have led to skewed and inaccurate results at best, and may have also been to the detriment of the patient's health.

Summary

Claims 2-12 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bosma in view of Sibille et al. Claim 13 is allowable because it teaches amplification primer pairs which are not found in the prior art, but is objected to for depending from a rejected claim.

Response to Arguments

5. Applicant's arguments filed February 4, 2002 have been fully considered but they are not persuasive. In particular, Applicant has argued that the reference of Bosma does not teach instructions for use. This argument is moot, however, in light of the 103 rejection of Bosma in view of Stratagene.

Applicant also argues that the rejection of claims 1-11 (now 2-11 and 14) is inappropriate because ther5e is no indication whatsoever in Bosma that Gilbert's Syndrome may affect the outcome of clinical drug trials. However, Sibille et al. teaches that patients with subclinical illness might be excluded, who might adversely influence interpretation of the results. Furthermore, Sibille teaches screening patients with a wide variety of clinical and subclinical illnesses, including those that have abnormal bilirubin amounts. Applicant has argued that patients with Gilberts Syndrome do not always have abnormal bilirubin levels. However, they do have a disease which may affect the outcome of clinical trials, depending of course on what the trial was for. If various medications were being tested that affected bilirubin levels, however, one of ordinary skill in the art would have been motivated to at least identify, if not exclude, those with Gilbert's Syndrome. Furthermore, since a way of rapidly screening for the disease was known in the art, as per Bosma, they would have been motivated to use it. Applicant has also argued that the methods used to identify patients with Gilbert's Syndrome were not those typically used to determine those with G.S. The Applicant goes on to give the example of individuals being required to abstain from alcohol and drugs for a period of 5 days prior to performing the analysis. However, those limitations are not found within the claims and therefore cannot be read into them. As presently worded, the claims recite only that a genetic "screen" is performed on the participants and no requirements are given for their behavior prior to the test. Applicant also argues that since the invention does not choose to necessarily exclude individuals from the clinical trial but rather identifies them, it does not exclude any significant part of the population. In claim

4, however, Applicant claims that the participants may be excluded on this basis. Furthermore, it would have been obvious that once the individuals were screened, the practitioner would have been able to make a decision whether to include them in the trial or not, based on what was being tested and what the desired outcome was. The practitioner may or may not count them as being a "healthy volunteer."

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janell Taylor Cleveland, whose telephone number is (703) 305-0273.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (703) 308-1152.

Any inquiries of a general nature relating to this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Group 1634 via the PTO Fax Center using (703) 872-9306 or 872-9307 (after final). The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989.)

Janell Taylor Cleveland

February 27, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600